REMARKS

Claims 17-32 are pending. Claims 17-25 and 29-32 are canceled. Claim 25 is amended to clarify the steps of the claimed method. Claim 28 is amended to omit the phrase "one of." Claim 27 is amended to remove reference to a bacterial ubiquitin promoter.

The amendments to claim 25 are supported by the specification and claims as filed, for example, by paragraphs [0030], [0041] through [0044], and by Table 2 of the specification. In particular, for example, Table 2 shows targeting efficiencies of a first targeting construct having a PGK promoter and a second targeting construct having a ubiquitin promoter (Table 2, col. 2), wherein the first and the second targeting constructs are directed to the same chromosomal location (Table 2, col. 1); a first and a second group of targeted mouse ES cells (Table 2, col. 3, per chromosomal location of col. 1); and the specification discloses that targeting efficiency is obtained by targeted gene modifications due to targeted, non-random insertions (paragraph [0030], paragraph [0043]).

The amendments to the claims add no new matter, and the Examiner is respectfully requested to enter them.

Rejections Under 35 USC § 103(a)

The Examiner maintained his rejection of claims 17-32, asserting that the rejected claims are obvious in light of Rohozinski et al. (2002) Genesis, 32:1-7, in view of Tsirigotis et al. (2001) BioTechniques, 31:120-130 and Ghazizadeh et al. (1998) J. Invest. Dermat. 111:492-496, for the reasons stated in the Office Actions dated 28 August 2006 and 05 June 2007.

In light of the amendments to the claims, Applicants submit that the Examiner's rejections are moot. To the extent that the references cited and arguments made by the Examiner might be applied to the amended claims, Applicants address them below.

Applicants refer the Examiner to the arguments made in Applicants' Amendment and Reply dated 05 October 2007 in support of patentability of the rejected claims, which Applicants also apply to the amended claims. In support of patentability of the amended claims, Applicants refer the Examiner to the enclosed Declaration of David Frendewey, a co-inventor of the claimed invention and a person of skill in the art to which the invention pertains, dated 01 April 2008.

As set forth in the enclosed Frendewey Declaration, the prior art provided no guidance to a person of ordinary skill for replacing a PGK promoter in a targeting construct with a ubiquitin promoter in a method for achieving improved targeting efficiency at a specific chromosomal

location in a mouse ES cell. See the enclosed Frendewey Declaration at ¶¶ 6-15.

As set forth in the enclosed Frendewey Declaration, a person of ordinary skill would conclude that the ubiquitin promoter's ability to drive expression in many cells and tissue types provides no guidance as to the ability of a ubiquitin promoter (1) to drive expression at a specific chromosomal location, and (2) to increase targeting efficiency to a specific chromosomal location in a targeting vector. See the enclosed Frendewey Declaration at ¶¶ 10 and 12.

As set forth in the enclosed Frendewey Declaration, the amended claims recite a method that provides surprising and unexpected results. A person of ordinary skill would find it surprising and unexpected that a replacing a PGK promoter driving a drug resistance gene in a targeting construct would lead to higher targeting efficiency at a specific chromosomal location, wherein the location is a location where the PGK and ubiquitin promoters each drive about the same level of expression of a drug resistance gene as measured in a quantitative in vitro assay. See the enclosed Frendewey Declaration at ¶¶ 16-23.

For the reasons stated above and in the enclosed Frendewey Declaration, Applicants submit that the claimed invention was not obvious to a person of ordinary skill at the time the invention was made.

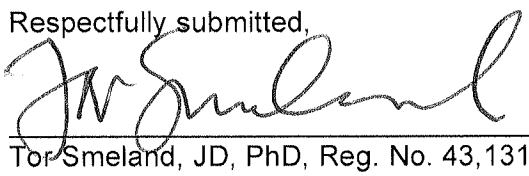
Conclusion

It is believed that this document is fully responsive to the Office action dated 01 November 2007. It is believed that the claims are in condition for allowance, and such action is respectfully urged.

Fees

Applicants submit that no fee other than the fee for a two-month extension is due. If any further fees are due, or overpayment has been made, please charge, or credit, Deposit Account No. 18-0650 in the amount of the overpayment or fee deficiency.

Respectfully submitted,



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